

AMENDMENT TO THE CLAIMS

Please cancel claims 1 – 7 and 17 – 47, and add new claims 48 – 69, as listed in the following claims:

Claim 1. (canceled) A method of mapping a pathway of differentiation of a population of embryonic cells, comprising:

- (i) selecting: (a) a set of gene expression products, wherein each gene expression product in the set is characteristic of a cell type that has undergone differentiation, such that a plurality of differentiated cell types are represented in the set; and (b) an exogenous factor from a library of exogenous factors;
- (ii) applying the exogenous factor to the population of embryonic cells;
- (iii) characterizing the effect of the exogenous factor on the differentiation pathway of the population of cells by determining gene expression products in the set; and
- (iv) mapping the pathway of differentiation of the cells.

Claim 2. (canceled) A method according to claim 1, wherein the set of expression products comprises at least one gene expression product that is expressed in a tissue selected from the mesoderm, ectoderm and endoderm.

Claim 3. (canceled) A method according to claim 1, wherein the set of expression products, comprises: at least one gene expression product expressed in the ectoderm, at least one gene expression product expressed in the mesoderm and at least one gene expression product expressed in the endoderm.

Claim 4. (canceled) A method according to claim 2 or 3, wherein the at least one gene expression product expressed in the ectoderm includes any of the group consisting of NF-H, keratin and adrenal D β H.

Claim 5. (canceled) A method according to claim 2 or 3, wherein the at least one gene expression product expressed in the mesoderm includes any of the group consisting of enolase, renin, CMP, kallikrein, WTI, cACT, δ -globulin and β -globulin.

Claim 6. (canceled) A method according to claim 2 or 3, wherein the at least one gene expression product expressed in the endoderm includes any of the group consisting of albumin, α 1AT, amylase, PDX-1, insulin and α FP.

Claim 7. (canceled) A method according to claim 1, wherein the exogenous factor is selected from a group consisting of interleukins, bFGF, TGF β 1, activin-A, BMP-4, HGF, EGF, β NGF and retinoic acid.

Claim 8. (previously presented) A method of directing differentiation of human embryonic cells to a specific cell type, comprising:

- a. permitting a population of human embryonic stem cells to form embryoid bodies *in vitro*;
- b. dissociating the embryoid bodies to provide embryonic cells for differentiating in the presence of at least one exogenous factor for an effective period of time; and
- c. causing directed differentiation of said embryonic cells to form the specific cell type.

Claim 9. (Original) A method according to claim 8, wherein the embryoid bodies are formed in a suspension culture.

Claim 10. (Original) A method according to claim 8, wherein the embryonic cells are monolayer cultures.

Claim 11. (Original) A method according to claim 8, wherein the exogenous factor is a growth factor.

Claim 12. (Original) A method according to claim 8, wherein the exogenous factor is an interleukin.

Claim 13. (Original) A method according to claim 11, wherein the exogenous factor is nerve growth factor.

Claim 14. (Original) A method according to claim 8, wherein the exogenous factor is retinoic acid.

Claim 15. (Original) A method according to claim 8, wherein the differentiated cells are neuronal cell type.

Claim 16. (Original) A method according to claim 15, wherein the differentiated cells have neuronal processes.

Claim 17. (canceled) A method according to claim 1, wherein the embryonic cells are human embryonic cells.

Claim 18. (canceled) A method of treating a subject suffering from a condition associated with degeneration of cells or malfunction of cells, comprising:

- a. accessing human embryoid body dissociated cells;
- b. treating the cells with an exogenous factor;
- c. causing the cells to differentiate; and
- d. placing an effective amount of differentiated cells into the subject to treat the condition.

Claim 19. (canceled) A method according to claim 18, wherein the condition is a heart condition in which heart muscle is degenerated.

Claim 20. (canceled) A method according to claim 19, wherein the cells are treated

with at least one exogenous factor selected from the group consisting of TGF- β , FGF, RA, HGF and EGF.

Claim 21. (canceled) A method according to claim 18, wherein the condition is a kidney condition in which kidney tissue is degenerated.

Claim 22. (canceled) A method according to claim 21, wherein the cells are treated with NGF.

Claim 23. (canceled) A method according to claim 18, wherein the condition is a skin condition in which skin tissue is degenerated.

Claim 24. (canceled) A method according to claim 23, wherein the cells are treated with BMP-4.

Claim 25. (canceled) A method according to claim 18, wherein the condition is a liver condition in which liver tissue is degenerated.

Claim 26. (canceled) A method according to claim 25, wherein the cells are treated with NGF.

Claim 27. (canceled) A method according to claim 18, wherein the condition is a brain condition in which brain tissue is degenerated.

Claim 28. (canceled) A method according to claim 27, wherein the cells are treated with at least one of
NGF or RA.

Claim 29. (canceled) A method according to claim 18, wherein the condition is a spinal cord injury in which neurons are degenerated.

Claim 30. (canceled) A method according to claim 29, wherein the cells are treated with at least one of NGF or RA.

Claim 31. (canceled) A method according to claim 18, wherein the condition is anemia or immunodeficiency.

Claim 32. (canceled) A method according to claim 18, wherein the cells are treated with at least one of NGF or interleukin.

Claim 33. (canceled) A method according to claim 18, wherein the condition is an adrenal condition in which adrenal tissue is degenerated.

Claim 34. (canceled) A method according to claim 33, wherein the cells are treated with RA.

Claim 35. (canceled) A method according to claim 18, wherein the subject is a human subject.

Claim 36. (canceled) A method according to claim 18, wherein the subject is a mammal.

Claim 37. (canceled) A method according to claim 18, wherein the selected cell type may be any of brain cells, liver cells, pancreatic cells, muscle cells, chondrocytes, kidney cells, Mullerian duct cells, heart cells, blood cells, skin cells and adrenal cells.

Claim 38. (canceled) A kit for determining differentiation pathways, comprising:

- (a) a plurality of sets of cell specific markers forming a panel in an assay format, the assay format including reagents for detecting the cell specific markers, the cell specific markers including a first set of markers that are characteristic of each of the ectoderm, mesoderm and endoderm of the embryo, and a second set of

markers that are characteristic of a body tissue, the second set containing more than one marker; and

(b) means for detecting reagents bound to cell specific markers.

Claim 39. (canceled) A kit according to claim 38, wherein the reagents are selected from DNA primers and antibodies.

Claim 40. (canceled) A method according to claim 38, wherein the means for detecting reagents bound to cell specific markers is selected from a gel based system, an immune detection assay and a solid chemistry assay.

Claim 41. (canceled) A method for screening an exogenous factor to determine whether the factor is capable of causing directed differentiation in a population of human embryonic cells, comprising:

- (a) subjecting the population of cells to the exogenous growth factor;
- (b) measuring the expression of receptors, the receptors being of a type that characterizes a particular differentiated cell population; and
- (c) determining whether the exogenous factor enhances differentiation,

maintains differentiation at a normal level or inhibits differentiation of the cell population.

Claim 42. (canceled) A panel of cell type differentiation determining markers, comprising: a set of reagents for specifically detecting gene expression of a plurality of ectodermal specific proteins, a plurality of mesodermal specific proteins and a plurality of endodermal specific proteins.

Claim 43. (canceled) A panel according to claim 40, wherein the ectodermal specific proteins, further comprise: proteins selected from the group consisting of : neurofilament protein, keratin and adrenal dopamine β hydroxylase.

Claim 44. (canceled) A panel according to claim 40, wherein the mesodermal specific proteins, further comprise: proteins selected from the group consisting of enolase, CMP, renin, kallikrein, WTI, cACT, β globin, δ globin and cActin.

Claim 45. (canceled) A panel according to claim 40, wherein the endodermal specific proteins further comprise: proteins selected from the group consisting of amylase, α -FP, PDX-1 and insulin.

Claim 46. (canceled) A panel according to claim 40, wherein the reagents are DNA primers.

Claim 47. (canceled) A panel according to claim 40, wherein the reagents are antibodies.

Claim 48. (new) A method of directing differentiation of human embryonic cells to human ectoderm cells, comprising:

- a. permitting a population of human embryonic stem cells to form embryoid bodies *in vitro*;
- b. dissociating the embryoid bodies to provide embryonic cells for differentiating in the presence of at least one exogenous factor for an effective period of time; and
- c. causing directed differentiation of said embryonic cells to form human ectoderm cells.

Claim 49. (new) A method according to claim 48, wherein, in causing, said embryonic cells form human epidermal skin cells.

Claim 50. (new) A method according to claim 49, wherein, in dissociating, the at least one exogenous factor includes EGF.

Claim 51. (new) A method according to claim 48, wherein, in causing, said

embryonic cells form human brain cells.

Claim 52. (new) A method according to claim 51, wherein, in dissociating, the at least one exogenous factor includes at least one of RA and NGF.

Claim 53. (new) A method according to claim 48, wherein, in causing, said embryonic cells form human adrenal cells.

Claim 54. (new) A method according to claim 53, wherein, in dissociating, the at least one exogenous factor includes RA.

Claim 55. (new) A method of directing differentiation of human embryonic cells to human endoderm cells, comprising:

- a. permitting a population of human embryonic stem cells to form embryoid bodies *in vitro*;
- b. dissociating the embryoid bodies to provide embryonic cells for differentiating in the presence of at least one exogenous factor for an effective period of time; and
- c. causing directed differentiation of said embryonic cells to form human endoderm cells.

Claim 56. (new) A method according to claim 55, wherein, in causing, said embryonic cells form human liver cells.

Claim 57. (new) A method according to claim 56, wherein, in dissociating, the at least one exogenous factor includes at least one of HGF and NGF.

Claim 58. (new) A method according to claim 55, wherein, in causing, said embryonic cells form human pancreatic cells.

Claim 59. (new) A method according to claim 58, wherein, in dissociating, the at

least one exogenous factor includes at least one of HGF and NGF.

Claim 60. (new) A method of directing differentiation of human embryonic cells to human mesoderm cells, comprising:

- a. permitting a population of human embryonic stem cells to form embryoid bodies *in vitro*;
- b. dissociating the embryoid bodies to provide embryonic cells for differentiating in the presence of at least one exogenous factor for an effective period of time; and
- c. causing directed differentiation of said embryonic cells to form human mesoderm cells.

Claim 61. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human chondrocytes.

Claim 62. (new) A method according to claim 61, wherein, in dissociating, the at least one exogenous factor includes BMP-4.

Claim 63. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human kidney cells.

Claim 64. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human Mullerian duct cells.

Claim 65. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human blood cells.

Claim 66. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human heart muscle cells.

Claim 67. (new) A method according to claim 66, wherein, in dissociating, the at

least one exogenous factor includes at least one of TGF- β and activin-A.

Claim 68. (new) A method according to claim 60, wherein, in causing, said embryonic cells form human skeletal muscle cells.

Claim 69. (new) A method according to claim 68, wherein, in dissociating, the at least one exogenous factor includes at least one of TGF- β and activin-A.